No. 25-1279

In The United States Court of Appeals
For the Fourth Circuit

PFLAG, INC., ET AL.,

Plaintiffs-Appellees,

– v. –

DONALD J. TRUMP, IN HIS OFFICIAL CAPACITY AS PRESIDENT OF THE UNITED STATES, ET AL.,

Defendants-Appellants.

ON APPEAL FROM THE UNITED STATES DISTRICT COURT FOR THE DISTRICT OF MARYLAND (No. 8:25-cv-00337)

BRIEF OF *AMICUS CURIAE* DO NO HARM, INC., IN SUPPORT OF THE UNITED STATES AND REVERSAL

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As Amicus Curiae

August 1, 2025

UNITED STATES COURT OF APPEALS FOR THE FOURTH CIRCUIT

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No. 25-1279 Caption: PFLAG, Inc., et al. v. Donald J. Trump, et al.

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(name of party/amicus)

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2. Does party/amicus have any parent corporations? ☐ YES ☑ NO
If yes, identify all parent corporations, including all generations of parent corporations:

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If yes, identify all such owners:

4. Is there any other publicly held corporation or other publicly held entity that has a direct financial interest in the outcome of the litigation? ☐YES ☑NO
If yes, identify entity and nature of interest:

5. Is party a trade association? (amici curiae do not complete this question) ☐YES ☑NO
If yes, identify any publicly held member whose stock or equity value could be affected substantially by the outcome of the proceeding or whose claims the trade association is pursuing in a representative capacity, or state that there is no such member:

6. Does this case arise out of a bankruptcy proceeding? ☐YES ☑NO
If yes, the debtor, the trustee, or the appellant (if neither the debtor nor the trustee is a party) must list (1) the members of any creditors' committee, (2) each debtor (if not in the caption), and (3) if a debtor is a corporation, the parent corporation and any publicly held corporation that owns 10% or more of the stock of the debtor.

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Signature: /s/ David H. Thompson Date: August 1, 2025

Counsel for: Amicus Curiae Do No Harm, Inc.

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INTEREST OF *AMICUS CURIAE*[1]

Do No Harm, Inc., is a nonprofit membership organization that includes over 27,000 physicians, nurses, medical students, patients, and policymakers. Do No Harm is committed to ensuring that the practice of medicine is driven by scientific evidence rather than ideology. In recent years, the practice of biology-denying interventions, euphemistically known as "gender affirming care," has become more common despite the serious harm caused by those medical interventions and the complete lack of reliable evidence for any benefit caused by them. Indeed, Do No Harm has released a database demonstrating that nearly 14,000 minors were subjected to biology-denying interventions in the United States between 2019 and 2023. *See Do No Harm Launches First National Database Exposing the Child Trans Industry*, DO NO HARM (Oct. 8, 2024), https://perma.cc/JW24-3J6V.

Part of Do No Harm's mission is to ensure that courts have a proper understanding of the dangers of these medical interventions and the lack of evidence supporting them. To that end, Do No Harm submits this brief to provide the Court with an accurate analysis of the lack of evidence justifying the use of puberty blockers, cross-sex hormones, and surgeries as treatments for gender dysphoria.

[1] All parties have consented to the filing of this brief. No counsel for any party authored this brief in whole or in part, and no entity of person, aside from *amicus curiae*, its members, or its counsel, made any monetary contribution intended to fund the preparation or submission of this brief.

INTRODUCTION

"Gender affirming care" is a medical scandal. This purported "treatment" calls for a host of biology-denying medical interventions from puberty blockers to cross-sex hormones to genital surgeries. All this to treat a *psychological* condition. These interventions inflict grave harms, and there is no reliable evidence demonstrating that they improve, much less resolve, gender dysphoria.

The lack of evidence of benefit from these interventions has been established in every systematic review to analyze the question. These reviews—which represent the highest form of medical evidence—have been conducted by health authorities in Finland, Sweden, the U.K., and by expert researchers hired by the health authority in the State of Florida and the U.K.'s National Health Service. All of them have concluded that no reliable evidence demonstrates that these interventions help resolve gender dysphoria. Following suit, the President's executive order, *Protecting Children from Chemical and Surgical Mutilation*, is justified by the known harms of these interventions—including the sterilization of healthy boys and girls—and the complete lack of evidence showing that they do anything to resolve gender dysphoria.

In this case, the district court largely ignored not only systematic reviews, but also the basic principles of evidence-based medicine. The court claimed that it was merely applying (since-vacated) circuit precedent. Yet it still chose to wade into the

factual debate. Upon doing so, it lost its footing and misstated the medical evidence about gender transition procedures, contradicting the conclusion of every systematic review that has been published.

If that were not enough, the district court also discounted a report based on a systematic review by citing a press release from a medical interest group, WPATH. But organizations like that one are motivated by ideology, not science, as revealed by their public statements on everything from critical race theory to gun control, and affirmative action to nuclear weapons—matters for which they have no expertise. Based on the current state of medical evidence, the President is correct in taking actions to limit the use of puberty blockers, cross-sex hormones, and surgeries to treat gender dysphoria in minors.

ARGUMENT

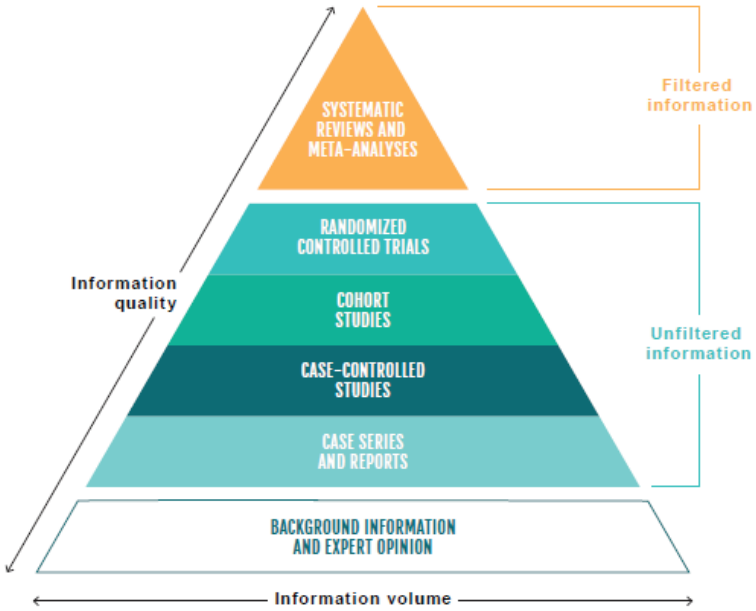
The district court misunderstood the evidence about experimental gender medicine. At first, it claimed to be mechanically applying (now vacated) precedent. *See PFLAG, Inc. v. Trump*, 769 F. Supp. 3d 405, 416 (D. Md. 2025) (citation omitted). But the court did not stop there. It went on to assert that medical interventions for children with gender dysphoria are "high-quality health care" and "medically necessary." *Id.* at 416-17. It then enjoined enforcement of an executive order intended to protect children. *See id.* at 454-55. For multiple reasons, that decision was a mistake. First, the district court ignored the systematic reviews—the

gold-standard of medical evidence—which all reveal fatal flaws in the evidence about the medical interventions at issue. And second, having ignored these systematic reviews, the court instead (a) offered bare assertions about the quality of medical evidence, and (b) relied on ideological position statements from medical interest groups. As a result, the court's analysis of the medical evidence should be rejected and its injunction vacated.

I. In The Practice Of Evidence-Based Medicine, Systematic Reviews Are The Highest Form Of Medical Evidence.

Although the proper practice of medicine is driven by evidence, not all medical evidence is created equal. Researchers have thus spent decades refining the process that clinicians use to assess the medical evidence supporting a particular medical intervention. That process—often referred to as the practice of "evidence-based medicine"—outlines a hierarchy of medical evidence based on the confidence a clinician can place in a particular source of evidence. *See* GORDON GUYATT ET AL., USERS' GUIDES TO THE MEDICAL LITERATURE: ESSENTIALS OF EVIDENCE-BASED CLINICAL PRACTICE 15 fig. 2-3, JAMAEVIDENCE (3d ed. 2015) ("Evidence-Based

Medicine User Guide"). The "pyramid of standards of evidence" reflects the hierarchy of reliability for evidence in medicine:



See Independent Review of Gender Identity Services for Children and Young People: Final Report at 55, NAT'L HEALTH SERV. ENG. (Apr. 2024), https://perma.cc/KM5C-49EZ ("Cass Review"). As the pyramid shows, "systematic reviews" are at the top of the hierarchy of medical evidence. At the bottom of the hierarchy is clinical experience—*i.e.*, "the unsystematic observations of individual clinicians." Evidence-Based Medicine User Guide at 15.

Systematic reviews provide the greatest insight into the medical evidence underpinning a particular intervention because they account for all relevant studies, assess those individual studies for areas of potential scientific bias, and thus show the *reliability* of the *entire* evidence base. *See id.* at 274-76. To assess bias in

individual studies, researchers frequently use tools such as the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) method. *See id.* at 16-17. In the GRADE system, researchers rate the evidence using specified criteria. "In the context of a systematic review, the ratings of the quality of evidence reflect the extent of our confidence that the estimates of the effect are correct." Howard Balshem et al., *GRADE Guidelines: 3. Rating the Quality of Evidence*, 64 J. CLINICAL EPIDEMIOLOGY 401, 403 (2011). This resulting rating of the evidence is either "high, moderate, low, or very low." Evidence-Based Medicine Users Guide at 16. The following definitions explain what the various levels mean:

> High Quality Evidence: "We are *very confident* that the true effect lies close to that of the estimate of the effect."
>
> Moderate Quality Evidence: "We are *moderately confident* in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different."
>
> Low Quality Evidence: "Our *confidence* in the effect estimate *is limited*: The true effect may be *substantially different* from the estimate of the effect."
>
> Very Low Quality Evidence: "We have *very little confidence* in the effect estimate: The true effect *is likely to be substantially different* from the estimate of effect."

Balshem, *supra*, at 404 tbl.2 (emphasis added). Thus, when evidence is deemed "low" or "very low" quality, that means researchers have "limited" or "very little confidence" that the results of the study reflect the truth; indeed, the truth may or *likely* will turn out "to be substantially different" from what such studies say.

Finally, after analyzing all relevant studies, the researchers will "summarize the results." Evidence-Based Medicine User Guide at 275. This process can include a quantitative synthesis or "meta-analysis" of data that provides an overview to clinicians. *See id.* at 275-76. The end result is a study of studies—a comprehensive look at the evidence on a given question that accounts for the reliability of the studies forming the evidence base.

In short, systematic reviews are the most reliable form of medical evidence. And for several reasons, they are substantially more reliable than narrative reviews (such as a clinician's experiences recounted in a declaration or expert-witness report). First, unlike systematic reviews, narrative reviews "have no explicit criteria for selecting the included studies." *Id.* at 273. Therefore, narrative reviews can cherry-pick examples and individual studies—discussing only those that support their conclusions and ignoring those that do not. Systematic reviews do not suffer from this flaw.

Second, narrative reviews "do not include systematic assessments of the risk of bias associated with primary studies." *Id.* (emphasis omitted). Thus, narrative reviews may stress that several studies all support the same conclusion, but "[c]onsistent results are less compelling if they come from studies with a high risk of bias than if they come from studies with a low risk of bias." *Id.* at 283. Systematic reviews account for this principle; narrative reviews do not. For these reasons

(among others), systematic reviews represent the highest form of medical evidence, and "optimally effective evidence-based practice dictates bypassing the critical assessment of primary studies and, if they are available, moving straight to the evaluation of rigorous systematic reviews." *Id.* at 4 (emphasis omitted).

II. Every Systematic Review Of Medical And Surgical Interventions For Minors With Gender Dysphoria Has Concluded The Evidence Is Weak.

Several entities and institutions have conducted systematic reviews to assess the evidence underlying the use of puberty blockers and cross-sex hormones as a treatment for minors with gender dysphoria. All have concluded that the evidence underlying medical interventions for gender dysphoria in minors is weak; zero have come out the other way.

1. *Finland*. The first systematic review came in 2019 when Finland's Ministry of Social Affairs and Health completed its review of the medical evidence. In light of this evidence review, Finland's healthcare authority concluded that "gender reassignment of minors is an experimental practice." *Recommendation of the Council for Choices in Health Care in Finland (PALKO/COHERE Finland): Medical Treatment Methods for Dysphoria Related to Gender Variance in Minors* at 8, PALVELUVALIKOIMA (Nov. 6, 2020), https://perma.cc/PF72-H654 (unofficial translation by the Society for Evidence Based Gender Medicine (SEGM)). This

conclusion was based on the fact that "[t]he reliability of the existing studies" is "highly uncertain." *Id*. at 7.

2. *The Cass Review Interim Report*. Next, in 2020, the United Kingdom's National Institute for Health and Care Excellence (NICE) completed its review of the evidence for using puberty blockers and cross-sex hormones on minors with gender dysphoria to aid the Cass Review, an independent review commissioned by the United Kingdom's National Health Service. *See NICE Evidence Reviews*, THE CASS REV., https://perma.cc/APZ2-W8MS. The result was two separate systematic reviews—one for puberty blockers and one for cross-sex hormones. *Evidence Review: Gonadotrophin Releasing Hormone Analogues for Children and Adolescents with Gender Dysphoria*, NAT'L INST. FOR HEALTH & CARE EXCELLENCE (Oct. 2020), https://perma.cc/F9FF-ZPFR ("NICE – Review of Puberty Blockers"); *Evidence Review: Gender-Affirming Hormones for Children and Adolescents with Gender Dysphoria*, NAT'L INST. FOR HEALTH & CARE EXCELLENCE (Oct. 2020), https://perma.cc/U49T-JLGJ ("NICE – Review of Cross-Sex Hormones"). The review of puberty blockers concluded that the relevant studies were "all small, uncontrolled observational studies, which are subject to bias and confounding, and all the results are of very low certainty using [a] modified GRADE" methodology. NICE – Review of Puberty Blockers at 13. Similarly, in the review of cross-sex hormones, NICE concluded that the relevant studies were "uncontrolled

observational studies, which are subject to bias and confounding and were of very low certainty using [a] modified GRADE" methodology. NICE – Review of Cross-Sex Hormones at 13.

3. *The State of Florida*. In 2022, researchers at Canada's McMaster University—a world-renowned institution in evidence-based medicine—completed a systematic review at the request of the Florida Agency for Health Care Administration. *See* Romina Brignardello-Petersen & Wojtek Wiercioch, *Effects of Gender Affirming Therapies in People with Gender Dysphoria: Evaluation of the Best Available Evidence* 5 (May 16, 2022), https://perma.cc/S4A3-NKDY. They too found that the evidence supporting these interventions was weak. "Due to the important limitations in the body of evidence," they concluded, "there is great uncertainty about the effects of puberty blockers, cross-sex hormones, and surgeries in young people with gender dysphoria." *Id*.

4. *Sweden*. In 2023, Swedish researchers published a systematic review that was commissioned by Sweden's Agency for Health Technology and Assessment of Social Services. *See* Jonas F. Ludvigsson et al., *A Systematic Review of Hormone Treatment for Children with Gender Dysphoria and Recommendations for Research*, 112 ACTA PAEDIATRICA 2279 (2023), https://perma.cc/E7S9-7CLB. The review concluded that the "[e]vidence to assess the effects of hormone treatment" on (among other things) mental health in minors "with gender dysphoria is

insufficient." *Id.* at 2280. Specifically, it noted that "[l]ong-term effects of hormone therapy on psychosocial health are unknown," and using puberty blockers to treat gender dysphoria "should be considered experimental treatment." *Id.*

5. *The Cass Review Final Report*. Most recently, researchers from York University published a series of systematic reviews as part of the Cass Review. The York University researchers conducted systematic reviews of the evidence for both puberty blockers and cross-sex hormones. *See* Jo Taylor et al., *Interventions To Suppress Puberty in Adolescents Experiencing Gender Dysphoria or Incongruence: A Systematic Review*, ARCHIVES DISEASE CHILDHOOD 1 (2024), https://perma.cc/UFL5-7RPB ("Taylor – Puberty Blockers"); Jo Taylor et al., *Masculinising and Feminising Hormone Interventions for Adolescents Experiencing Gender Dysphoria or Incongruence: A Systematic Review*, ARCHIVES DISEASE CHILDHOOD 1 (2024), https://perma.cc/ACK3-XB8D ("Taylor – Cross-Sex Hormones"). In their review of puberty blockers, the researchers determined that their "findings add to other systematic reviews in concluding there is insufficient and/or inconsistent evidence about the effects of puberty suppression on gender dysphoria, body satisfaction, psychological and psychosocial health, cognitive development, cardiometabolic risk and fertility." Taylor – Puberty Blockers at 12. Similarly, in their review for cross-sex hormones, the researchers concluded that their "findings add to other systematic reviews in concluding there is insufficient

and/or inconsistent evidence about the risks and benefits of hormone interventions in this population." Taylor – Cross-Sex Hormones at 6.

To summarize, all these systematic reviews concluded the same thing: there is no reliable evidence to justify the use of puberty blockers and cross-sex hormones as a treatment for gender dysphoria in minors. And this conclusion comports with the findings of the experts in evidence-based medicine who were hired by the medical interest group WPATH—a group the district court invoked. *See PFLAG*, 769 F. Supp. 3d at 448. Specifically, the research team at Johns Hopkins University hired by WPATH reported that they "found 'little to no evidence about children and adolescents'" for these interventions. *See Trans Health Group Fought Study Analyzing 'Gender Affirming Care' for Children, Docs Show*, DO NO HARM (May 17, 2024), https://perma.cc/8UVR-5EZ3 (citation omitted).

III. The District Court Largely Ignored Systematic Reviews, Focusing Instead On Piecemeal Evidence And Policy Statements.

Instead of basing its preliminary injunction decision on systematic reviews—the gold-standard just described—the district court relied on two types of substitutes. First, the court made sweeping assertions about these biology-denying medical interventions. *See PFLAG*, 769 F. Supp. 3d at 416-17, 448 & n.41, 450. Yet these claims all fail under the principles of evidence-based medicine. Second, the court relied on a press release from medical interest group WPATH to ignore the Cass Review, a report grounded on a systematic review. *See id.* at 448. But medical

interest groups like WPATH base their opinions more on politics than science. Thus, neither of the court's stand-ins can alter the conclusion of every on-point systematic review—that there is no reliable evidence for the use of medical interventions to treat gender dysphoria in minors. *See supra*, at pp. 8-12.

A. The Court Misunderstood The Principles Of Evidence-Based Medicine And Thus Made Multiple Erroneous Assertions.

Below, *amicus* provides a selection of the district court's most flawed assertions—concerning suicide rates, evidence quality, and the Cass Review—followed by an explanation of why those assertions are wrong.

1. *Suicide Rates.* First, the district court claimed that the "risk of suicide" was an injury caused by "each day that passes" without a preliminary injunction. *Id.* at 450. This rhetoric is grossly irresponsible, supported by no data, and outright contradicted by Plaintiffs-Appellees' own experts. To start, even a researcher for WPATH admits this is wrong: "There is insufficient evidence to draw a conclusion about the effect of hormone therapy on death by suicide among transgender people." Kellan E. Baker et al., *Hormone Therapy, Mental Health, and Quality of Life Among Transgender People: A Systematic Review*, 5 J. ENDOCRINE SOC'Y 1, 13 tbl. 6 (2021), https://perma.cc/6D6Q-GDQA; *see also id.* at 12 ("It was impossible to draw conclusions about the effects of hormone therapy on death by suicide."). And just last year, in what is likely the most controlled environment that is currently feasible, a researcher in the U.K. concluded that there was no evidence of a rise in suicides

after the country's health service had restricted the use of puberty blockers as a treatment for gender dysphoria. *See Puberty Blocker Curb Has Not Led to Suicide Rise—Review*, BBC (July 20, 2024), https://perma.cc/J36J-HWLN.

Most alarmingly, just months ago, Plaintiffs-Appellees' leading experts, Drs. Antommaria and Shumer, *see* Decl. of Dr. Antommaria, *PFLAG, Inc. v. Trump*, No. 8:25-cv-00337-BAH (D. Md. Feb. 18, 2025), Dkt. 69-48 ("Antommaria Decl."); Decl. of Dr. Shumer, *PFLAG, Inc. v. Trump*, No. 8:25-cv-00337-BAH (D. Md. Feb. 18, 2025), Dkt. 69-50 ("Shumer Decl."), said precisely the opposite of the claims the district court endorsed in its opinion. Specifically, the court repeatedly invoked the "risk of suicide" as a harm resulting from the executive order. *PFLAG*, 769 F. Supp. 3d at 450. But in litigation over a law restricting the practice of these very same interventions, Plaintiffs-Appellees' expert Dr. Shumer had the following to say:

> Q. And you agree there is no data linking gender-affirming care to a reduction in suicide, correct?
>
> …
>
> A. Yes, I don't believe that there is strong data linking gender-affirming care in youth to an outcome of less completed suicides.

Dep. Tr. of Dr. Shumer, *Misanin v. Wilson*, No. 2:24-cv-4734-RMG (D.S.C. Oct. 31, 2024), Dkt. 46-3 at 157:4-10 ("Shumer *Misanin* Tr."). Dr. Antommaria echoed the same sentiment that there is no data linking these interventions to a reduction in suicide:

> Q. Can you name any study demonstrating that medical transition for adolescents reduces the rate of completed suicides among any population of transgender adolescents?
>
> …
>
> A. No, sir. I'm not aware of such a study.

See Dep. Tr. of Dr. Antommaria, *Misanin v. Wilson*, No. 2:24-cv-4734-RMG (D.S.C. Oct. 31, 2024), Dkt. 46-4 at 131:15-21 ("Antommaria *Misanin* Tr."). In short, the district court's claim that a "risk of suicide" results from the executive order is shocking given the actual data on this question. *PFLAG*, 769 F. Supp. 3d at 450.

2. *Evidence Quality.* Next, the district court asserted that experimental gender medicine is "high-quality health care." *Id.* at 416 (quotation marks omitted). It further claimed that risks of non-treatment are "supported by ample medical data." *Id.* at 448 n.41. Yet the parties all agree that the evidence for these interventions is weak; the disagreement is over whether that weakness matters. For instance, the district court cited one of Plaintiffs-Appellees' experts, Dr. Antommaria, who explains that recommendations for many interventions are made based on "low" or "very low" quality evidence under the GRADE methodology. *See* Antommaria Decl. ¶¶ 37-47. In particular, he compares the use of puberty blockers to treat central precocious puberty to the use of puberty blockers to treat gender dysphoria.

But the risks and benefits associated with different interventions for different conditions should not be conflated. *See* Evidence-Based Medicine User Guide at 6

(noting that providers must determine "the tradeoff among the benefits, risks, and burdens of alternative management strategies" (emphasis omitted)). Plaintiffs-Appellees' expert ignored this fundamental principle. Consider his key example: central precocious puberty. That treatment involves delaying puberty until the normal age, at which point the boy or girl will proceed through his or her *natural* puberty. *Precocious Puberty*, MAYO CLINIC, https://perma.cc/4FL2-9PL5 (noting that treatment may involve children receiving GnRH analogues "until they reach the usual age of puberty," at which point "the treatment stops" and "puberty starts again"). With biology-denying interventions, however, the patient's natural puberty is permanently suppressed by administering puberty blockers at later ages. The harms and risks of *never* going through natural puberty are vastly different from merely delaying one's natural puberty until the normal age. For example, unlike a child who takes puberty blockers to treat central precocious puberty, a gender dysphoric child whose puberty is suppressed and then continues on cross-sex hormones will be sterilized—as Plaintiffs-Appellees' own experts have admitted elsewhere. *See* Antommaria *Misanin* Tr. at 49:5-11 (admitting that a patient who proceeds from pubertal suppression to cross-sex hormones "would be anticipated to be infertile").

Indeed, the Supreme Court rejected this precise argument in *Skrmetti*. There, the challengers and dissent "contend[ed] that an adolescent whose biological sex is

female cannot receive puberty blockers or testosterone to live and present as a male, but an adolescent whose biological sex is male can" and vice-versa with estrogen. *United States v. Skrmetti*, 145 S. Ct. 1816, 1830 (2025). This argument, the Court concluded, "contort[ed] the meaning of the term 'medical treatment.'" *Id.* "Notably absent from their framing," the Court explained, "is a key aspect of any medical treatment: the underlying medical concern the treatment is intended to address." *Id.* "When, for example, a transgender boy (whose biological sex is female) takes puberty blockers to treat his gender incongruence, he receives a different medical treatment than a boy whose biological sex is male who takes puberty blockers to treat his precocious puberty." *Id.* In sum, the district court's claims about the "high-quality" of experimental gender medicine is not supported by even challengers' experts.

Moreover, the district court's position on the quality of the evidence is directly contradicted by those experts. For one, we cannot know about the long-term sexual implications of puberty blockers because, as one of Plaintiffs-Appellees' experts has explained, we have *no data* regarding patient outcomes after the age of 30 for adolescents who used puberty blockers followed by cross-sex hormones. Antommaria *Misanin* Tr. at 53:6-12 ("I'm not aware of any studies" that follow "individuals to their 30th birthday when measuring the safety or efficacy of puberty blockers followed by cross-sex hormones[.]").

Infertility is not the only risk the district court minimized. The following list highlights the numerous critical aspects of both gender dysphoria and these interventions that are wholly unknown—as demonstrated by the following admissions from Plaintiffs-Appellees' experts in litigation over these same issues:

- We do not know what causes gender dysphoria. Shumer *Misanin* Tr. 33:18-21.
- We cannot determine whether any particular individual with gender dysphoria will continue to be transgender in the future. *Id*. at 33:22-25.
- We have no idea what the long-term effects of pubertal suppression are on neurodevelopment. Antommaria *Misanin* Tr. 47:3-12.
- We do not understand why there has been a sudden and recent increase in the number of individuals with gender dysphoria. *Id*. at 30:9-31:7.
- We do not know why this increase has disproportionately affected females. *Id*. at 31:9-32:4.
- We do not know why there is an overrepresentation of individuals with an Autism Spectrum Disorder. *Id*. at 42:7-17; Shumer *Misanin* Tr. 27:20-28:2.
- We do not know if patients' bone mineral density will ever return to normal later in life after taking puberty blockers. Antommaria *Misanin* Tr. 45:17-46:7.

The United States is entirely justified in taking actions to limit the use of these dangerous and unproven interventions.

3. *The Cass Review.* Tripling down, the district court quoted the medical interest group WPATH for the proposition that the Cass Review—the systematic review discussed *supra*, at pp. 9-12—contains "'unfounded medical opinion[s]' that

'ignor[e] more than three decades of clinical experience.'" *PFLAG*, 769 F. Supp. 3d at 448 (quoting *Washington v. Trump*, 768 F. Supp. 3d 1239, 1274 (W.D. Wash. 2025)). Ironically, that allegation is itself unfounded and conflicts with Supreme Court precedent. Just weeks ago, the Court explained in *United States v. Skrmetti* the importance of the Cass Review in exposing that "the evidence concerning the use of puberty blockers and hormones to treat transgender minors" is "'remarkably weak,' concluding that there is 'no good evidence on the long-term outcomes of interventions to manage gender-related distress.'" 145 S. Ct. at 1836-37 (citation omitted). Writing for the Court, Chief Justice Roberts described the Cass Review as one of the "developments" that justifies "flexibility" when judicially analyzing restrictions on gender transition procedures. *Id.* at 1836. Breaking with the Court, the district court chose a rigid injunction instead of flexibility.

B. The Court Mistakenly Relied On The Opinions Of Politically Motivated Medical Interest Groups.

The district court also sought to replace systematic reviews with reliance on medical interest groups, as is revealed by its citation of WPATH to criticize the Cass Review. *See supra*, at pp. 9-12. Indeed, a collection of medical interest groups filed an *amici* brief at the district court. *See* Br. of *Amici Curiae* Am. Acad. of Pediatrics & Additional Nat'l & State Med. & Mental Health Orgs. in Support of Plaintiffs' Motion for Preliminary Injunction, *PFLAG, Inc. v. Trump*, No. 8:25-cv-00337-BAH (D. Md. Feb. 21, 2025), Dkt. 79-1 ("Medical Interest Group Br."). But that brief was

not a systematic review. And those organizations do not compensate for the district court's failure to engage with real systematic reviews. This is because ideology—not evidence-based medicine—guides decision-making within those interest groups.

Start with the *amicus* WPATH. "Recent revelations suggest that WPATH . . . bases its guidance on insufficient evidence and allows politics to influence its medical conclusions." *Skrmetti*, 145 S. Ct. at 1847 (Thomas, J., concurring). For example, "recent reporting has exposed that WPATH changed its medical guidance to accommodate external political pressure." *Id.* at 1848. Specifically, "a senior official in the Biden administration pressed WPATH to remove age limits for adolescent surgeries for care of transgender minors on the theory that specific listings of ages, under 18, will result in devastating legislation for trans care." *Id.* at 1848-49 (cleaned up). WPATH agreed to do so, thus underscoring that "'WPATH's lodestar is ideology, not science.'" *Id.* at 1848 (quoting *Eknes-Tucker v. Gov. of Ala.*, 114 F.4th 1241, 1261 (11th Cir. 2024) (Mem.) (Lagoa, J., concurring in denial of rehearing en banc)).

Next, consider *amicus* the American Academy of Child & Adolescent Psychiatry (AACAP). When it comes to the permanent and lifelong risks of experimental gender medicine, such as sterilization, AACAP believes that children and adolescents can provide informed consent to these treatments. *See* Medical Interest Group Br. at 7 (noting that "the patient" must give "informed consent" for

puberty blockers and cross-sex hormones). But when it came to lifetime prison sentences for minors, AACAP had this to say:

> Scientists have found that adolescents as a group, even at later stages of adolescence, are more likely than adults to engage in risky, impulsive, and sensation seeking behavior. This is, in part, because they overvalue short-term benefits and rewards, and are less capable of controlling their impulses, making them susceptible to acting in a reflexive rather than a planned voluntary manner. Adolescents are also more emotionally volatile and susceptible to stress and peer influences. In short, the average adolescent cannot be expected to act with the same control or foresight as a mature adult.

Br. for the Am. Academy of Child & Adolescent Psychiatry et al. as *Amici Curiae* Supporting Neither Party, *Miller v. Alabama*, 567 U.S. 460 (2012) (Nos. 10-9646, 10-9647), 2012 WL 121237, at *2-3. *Amicus* Do No Harm obviously takes no position on the merits of *Miller v. Alabama*. But AACAP's argument to the Supreme Court in that case cannot be squared with its argument to the district court regarding the capacity of children and adolescents to give informed consent to the high risk of sterilization that accompanies the use of puberty blockers and cross-sex hormones to treat gender dysphoria.

Instead, one is left with the distinct impression that something more than "science" is driving the bus. Indeed, the Medical Interest Group *Amici* consist almost entirely of repeat players who issue public policy statements on issue after issue that bears no relation to their purported expertise. Name a hot-button social issue, and they have issued formal positions on it.

a. Critical Race Theory? Check. *See Anti-Racism Resource Library*, AM. ACAD. OF CHILD & ADOLESCENT PSYCH. (Jan. 2023), https://perma.cc/Y5B6-RXNF; *ACOP Statement Against Structural Racism and Inequality*, AM. COLL. OF OSTEOPATHIC PEDIATRICIANS (June 4, 2020), https://perma.cc/6HG8-UPPL; *Anti-Racism & Equity Toolkit*, ACAD. PEDIATRIC ASS'N, https://perma.cc/ETT3-575S; *Call for Papers on the Impacts of Structural and Social Determinants of Health, Including Multiple Forms of Racism and Minoritization, in Child and Adolescent Mental Health*, J. AM. ACAD. OF CHILD & ADOLESCENT PSYCH. (2023), https://perma.cc/NP4C-37EE (calling for papers on "micro-aggressions" and "multiple forms of racism"); American Academy of Pediatrics Board of Directors, *Truth, Reconciliation, and Transformation: Continuing on the Path to Equity*, 146 PEDIATRICS 449, 451 (2020), https://perma.cc/BYW5-XU9V (reiterating organization's belief that "racism [i]s a core social determinant of health and a driver of health inequities" and stating its commitment to combatting "structural and systemic anti-Black racism" through its "equity agenda").

b. Gun Control? Check. *See* Press Release, Justin Worsley, *NAPNAP Position Statement on Prevention of Firearm Violence and Injury in Children*, NAT'L ASS'N OF PEDIATRIC NURSE PRACTITIONERS (Jan. 12, 2023), https://perma.cc/S3N3-NUQW; *American Academy of Nursing's Statement: Firearm Safety and Violence Prevention*, AM. ACAD. OF NURSING (Nov. 17, 2022), https://perma.cc/4BNS-UZDE;

The ACOP Supports The Call To ACTION Towards Common Sense Gun Regulation, AM. COLL. OF OSTEOPATHIC PEDIATRICIANS (June 1, 2022), https://perma.cc/55ZN-L3NB; *Policy Statement on Children and Guns*, AM. ACAD. OF CHILD & ADOLESCENT PSYCH., https://perma.cc/CWJ9-9UYU; Scott C. Denne et al., *Funding for Gun Violence Research: The Importance of Sustained Advocacy By Academic Pediatricians*, 87 PEDIATRIC RSCH. 800 (2020), https://perma.cc/9YRD-3VPN (from the Academic Pediatric Association, American Pediatric Society, and the Association of Medical School Pediatric Department Chairs); Robert M. McClean et al., *Firearm-Related Injury and Death in the United States: A Call to Action From the Nation's Leading Physician and Public Health Professional Organizations*, ANNALS OF INTERNAL MED. (2019), https://perma.cc/562U-C8LM (from the American Academy of Family Physicians, American Academy of Pediatrics and other groups); Letter from Susan Bostwick, Acad. Pediatric Ass'n President et al., to Rep. Stephanie Murphy (Apr. 2, 2018), https://perma.cc/VCQ6-QYE6 (from the Association of Medical School Pediatric Department Chairs and other groups); Letter from AANS/CNS Joint Section on Neurotrauma & Critical Care et al., to Patty Murray, U.S. Senate Comm. on Appropriations, Chairman (June 3, 2024), https://perma.cc/ALU6-P8R3 (from the American College of Obstetricians and Gynecologists, American College of Physicians, American Pediatric Society, American Academy of Family Physicians, Pediatric Endocrine Society, Association

of American Medical Colleges, Society for Adolescent Health and Medicine, among other groups).

c. Immigration? Check. *See* Letter from the American Pediatric Association et al., to Kristi Noem, U.S. Dep't of Homeland Sec., Secretary (Mar. 25, 2025), https://perma.cc/H29Z-8U66 (stating the position of the American Academy of Pediatrics, the American College of Obstetricians and Gynecologists, and other groups as to whether particular detention procedures are "necessary"); *AACAP Calls for Swift Congressional Passage of the "Dream Act"*, AM. ACAD. OF CHILD & ADOLESCENT PSYCH. (May 21, 2018), https://perma.cc/UH27-S6A3; *AACAP Statement on DACA Rescission*, AM. ACAD. OF CHILD & ADOLESCENT PSYCH. (Sep. 2017), https://perma.cc/XGS5-7D39; Press Release, AAP et al., *Leading Pediatric Medical Organizations Respond to Recent Executive Orders Impacting Immigrants and Refugees* (Feb. 14, 2017), https://perma.cc/J29C-EVZ9 (offering, in part, a policy position on border defenses from the Academic Pediatric Association, Association of Medical School Department Chairs, American Pediatric Society, among other groups); Letter from American College of Physicians et al., to John F. Kelly, U.S. Dep't of Homeland Sec., Secretary (Feb. 7, 2017), https://perma.cc/567A-44J5 (asserting the desire for "a process to admit refugees" from Syria of the American College of Physicians, Society for Adolescent Health and Medicine, and other organizations).

d. Climate Change? Check. *See European and Global Endocrine Community Call for Legislative Measures to Address Endocrine Disrupting Chemicals*, EUROPEAN SOC'Y FOR PAEDIATRIC ENDOCRINOLOGY (July 7, 2025), https://perma.cc/8NW7-N4FN (from the Endocrine Society, and others); *Climate Change and Climate Distress in Youth*, AM. ACAD. OF CHILD & ADOLESCENT PSYCH. (Mar. 2024), https://perma.cc/T4C3-EBNX; *Addressing Climate Change: Position Statement*, AM. COLL. OF OBSTETRICIANS & GYNECOLOGISTS (Nov. 2021), https://perma.cc/2R4X-E9KJ; National Association of Pediatric Nurse Practitioners et al., *NAPNAP Position Statement on the Effects of Climate Change on Children's Health: The Role of Pediatric-Focused Advanced Practice Registered Nurses*, 35 J. PEDIATRIC HEALTH CARE 621 (2021), https://perma.cc/F2VA-CGLJ; Jianhong Liu et al., *Policy Brief on Climate Change and Mental Health/Well-Being*, 68 NURSING OUTLOOK 517 (2020), https://perma.cc/C2CU-9NAN (from American Academy of Nursing); Samantha Ahdoot et al., *Climate Change and Children's Health: Building a Healthy Future for Every Child*, 153 PEDIATRICS 75 (2024), https://perma.cc/5KLL-LMWJ; Maya Earls, *Major Medical Groups Release Call to Action on Climate Change*, SCI. AM. (June 25, 2019), https://perma.cc/FVL5-GGQM (signed by the Academic Pediatric Association, American College of Physicians, American Academy of Family Physicians, among other groups).

e. Affirmative Action? Check. *See* Letter from American College of Physicians et al., to Sen. Joe Kennedy (Apr. 16, 2024), https://perma.cc/3NHQ-ZWQG (Endocrine Society and other groups arguing for "considering race and ethnicity" in selecting a student body); Br. for the Am. Med. Colls. et al. as *Amici Curiae* Supporting Respondents, *Students For Fair Admissions, Inc. v. President & Fellows of Harvard Coll.*, Nos. 20-1199, 21-707 (U.S. July 28, 2022), 2022 WL 3036400 (joined by American Academy of Child & Adolescent Psychiatry, American Academy of Family Physicians, American College of Obstetricians and Gynecologists, American College of Physicians, American Pediatric Society, among other groups); *ACOG Statement on Supreme Court Affirmative Action Ruling*, AM. COLL. OF OBSTETRICIANS & GYNECOLOGISTS (June 29, 2023), https://perma.cc/X2HX-CLR3.

f. Nuclear Weapons? Remarkably, yes. If anyone has ever wondered what the American Academy of Family Physicians thinks about nuclear weapons or biological warfare, the Medical Interest Group *Amici* have that covered too. *See Nuclear, Biological and Chemical (NBC) Warfare*, AM. ACAD. OF FAM. PHYSICIANS (2020), https://perma.cc/843P-76WB. Almost unbelievably, AAFP is not the only *amicus* to set forth its nuclear proliferation policy. Indeed, members of the AAP have even promulgated their view on "the pediatrician's role" in "taking a stand against nuclear proliferation." Thomas B. Newman, *Taking a Stand Against Nuclear*

Proliferation: The Pediatrician's Role, 121 PEDIATRICS e1430, e1430 (2008), https://perma.cc/9Q58-TVGT (cleaned up).

Lastly, although the American Psychological Association is not serving as *amicus* in this case, the Medical Interest Group *Amici* cite its work. *See* Medical Interest Group Br. at 3. Perhaps the Association has not joined the Medical Interest Group *Amici* here because it recognizes that its basis for previously opposing the death penalty for 18- to 20-year-olds also serves as a basis for opposing the provision of sterilizing treatments to children and adolescents. Just a few years ago, the Association adopted a resolution explaining that brains are not fully developed enough—even by age 20—to justify the imposition of the death penalty for eligible crimes:

> WHEREAS developmental neuroscience, including research on both the structure and function of brain development, establishes that significant maturation of the brain continues through at least age 20, especially in the key brain systems implicated in a person's capacity to evaluate behavioral options, make rational decisions about behavior, meaningfully consider the consequences of acting and not acting in a particular way, and to act deliberately in stressful or highly charged emotional environments, as well as continued development of personality traits (e.g., emotional stability and conscientiousness) and what is popularly known as 'character.'

APA Resolution on the Imposition of Death as a Penalty for Persons Aged 18 Through 20, Also Known As the Late Adolescent Class at 2, AM. PSYCH. ASS'N (Aug. 2022), https://perma.cc/7UG9-TWM6 (cleaned up). "[I]t is clear," the resolution continued, that "the brains of 18- to 20-year-olds are continuing to develop in key

brain systems related to higher-order executive functions and self-control," which includes "planning ahead, weighing consequences of behavior, and emotional regulation." *Id.* This reasoning is as good as any for acknowledging the children and adolescents are incapable of adequately consenting or assenting to the harms and risks associated with these treatments.

In sum, these groups are no substitute for systematic reviews. *Amicus* Do No Harm does not need to overstate the point: medical interest groups, like all other interest groups, are of course entitled to take policy positions on any range of topics—including those beyond the groups' expertise (such as nuclear armament). But given the track record of the Medical Interest Group *Amici* here, *see supra*, at pp. 19-28, it is hard to take seriously the proposition that these *amici* come forward to offer their humble opinion regarding the "science" and then return to their clinics. Rather, their *modus operandi* appears to be reaching a policy decision first and then backfilling the science to achieve their preferred policy outcome.

Therefore, this Court should not hesitate to say what the law is irrespective of what politically motivated medical interest groups insist—no matter how many of them line up to add their name to yet another recycled brief. Under the correct application of the Constitution and Supreme Court precedent, the President's executive order on the harmful and irreversible practice of experimental gender medicine on minors is indisputably constitutional.

CONCLUSION

For these reasons, this Court should vacate the preliminary injunction.

Dated: August 1, 2025

Respectfully submitted,

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CERTIFICATE OF COMPLIANCE

I, David H. Thompson, hereby certify that:

1. This brief complies with the type-volume limitations of Fed. R. App. P. 29(a)(5) because this brief contains 6,239 words, excluding the parts of the brief exempted by Fed. R. App. P. 32(f).

2. This brief complies with the typeface requirements of Fed. R. App. P. 32(a)(5) and the type style requirements of Fed. R. App. P. 32(a)(6) because this brief has been prepared in a proportionally spaced typeface using Microsoft Word using 14-point Times New Roman font.

Dated: August 1, 2025

/s/ David H. Thompson
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CERTIFICATE OF SERVICE

Pursuant to Fed. R. App. P. 25(d) and L.R. 25(b)(3), I hereby certify that on August 1, 2025, I electronically filed the foregoing with the Clerk of the Court for the United States Court of Appeals for the Fourth Circuit by using the CM/ECF system. I certify that all participants in the case are registered CM/ECF users and that service on counsel will be accomplished by the CM/ECF system.

Dated: August 1, 2025

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